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Diagnostic and therapeutic impact of ambulatory electrocardiography in acute stroke

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Abstract

Detection of paroxysmal atrial fibrillation (PAF) in patients with recent ischemic stroke or TIA suggests a cardioembolic etiology and leads to initiation of oral anticoagulation in suitable candidates. We assessed the diagnostic and therapeutic impact of adding ambulatory electrocardiography (24 hr ECG) to a standardised ischemic stroke workup.

Methods : We measured the frequency of detection of PAF in consecutive stroke patients who underwent 24 hr ECG that was not diagnosed clinically or on a standard 12-lead ECG.

Results : One hundred forty five ischemic stroke patients were included. 24 hr ECG was obtained in 136 patients (93.8%). Clinically unsuspected PAF was detected on 24 hr ECG in 7 patients (5.1%). The secondary prevention measure changed from antiplatelet agents to oral anticoagulation in 6 of 7 patients.

Conclusion : Our findings suggest that ambulatory electrocardiography is a valuable diagnostic tool in the workup of stroke patients. Further prospective studies are needed to identify subtypes of patients in whom the yield of ambulatory electrocardiography is higher.

Key words : Ambulatory electrocardiography ; ischemic stroke ; atrial fibrillation.

Several tests can be performed to diagnose and identify the etiology of cerebral ischemic symptoms, but how often these tests change the etiologic classification of stroke and influence therapeutic management is not very well defined (Hankey and Warlow, 1992). Ambulatory electrocardiography is a simple investigation to detect asymptomatic paroxysmal atrial fibrillation. Detection of this atrial arrhythmia suggests a cardioembolic etiology and changes the antithrombotic strategy from antiplatelet agents to oral anticoagulants (Anonymous, 1994 ; Albers, Dalen, *et al.*, 2001 ; Hart, Pearce, *et al.*, 2000 ; Lip, 1997). Despite these advantages ambulatory electrocardiography is not recommended as a routine diagnostic measure in the workup of ischemic stroke patients by many guidelines (Anonymous, 1989 ; Culebras, Kase, *et al.*, 1997 ; Feinberg, Albers, *et al.*, 1994 ; Hankey and Warlow, 1992 ; Limburg and Tuut, 2000).

The goal of our study was to establish the frequency of paroxysmal AF detected by ambulatory electrocardiography, which was not known by history or diagnosed on admission by a routine 12-lead ECG, and to evaluate the impact on the etiologic classification of stroke and on secondary prevention measures.

Methods

We performed a retrospective study of all ischemic stroke patients admitted to our Stroke Unit from March until November 2001, in whom a 24 hour ECG monitoring was obtained together with a standard diagnostic workup, consisting of extended laboratory tests, routine ECG on admission, imaging of the brain with CT scan, diffusion weighted imaging (DWI) and magnetic resonance angiography (MRA), echocardiography (TTE and/or TEE), carotid ultrasound and, if needed, cerebral angiography. Medical history, cerebrovascular risk factors and medications were recorded.

Acute ischemic stroke was defined as a focal neurological deficit of presumed vascular origin that lasted for at least 24 hours, or if symptoms lasted less than 24 hours, in whom an area of hyperintensity consistent with cerebral ischemia was found on DWI. Ambulatory electrocardiography results were analysed with Synetec software (Ela Medical, France). Paroxysmal atrial fibrillation was defined, as transient atrial fibrillation that was not documented on the ECG obtained at baseline and that was not known to have occurred in the two years prior to ischemic stroke.

The clinical presentation was classified according to the Bamford classification and the Trial of Org 10172 in Acute Ischemic Stroke Trial criteria were used to determine the etiologic classification of the strokes and the definition of high risk sources of cardiac embolism (Adams, Bendixen, *et al.*, 1993 ; Bamford, Sandercock, *et al.*, 1991). The etiology was evaluated without knowledge of the

Table 1

Major findings on echocardiography (TTE or TEE) in 140 patients

Abnormalities		n (%)
Masses	Atrial thrombi	2 (1.4%)
	Ventricular tumor	1 (0.7%)
Congenital heart disorders	PFO	9* (6.4%)
	Atrial septal aneurysm	2 (1.4%)
	Atrial septal defect	1 (0.7%)
	Tetralogy of Fallot	1 (0.7%)
Valvular disorders	Endocarditis	1 (0.7%)
	Mitral valve prolapse	1 (0.7%)
	Mitral stenosis	1 (0.7%)
	Mitral valve calcification	1 (0.7%)
	Significant mitral valvular insufficiency	1 (0.7%)
Contractility disorders	Ventricular regional hypokinesia or akinesia	15† (10.7%)
	Diffuse ventricular hypocontractility	2 (1.4%)
	Dilated cardiomyopathy	1 (0.7%)
Spontaneous echo contrast		10 (7.1%)
Aortic atheromatosis		4 (2.9%)

* One patient had both a PFO and ventricular hypokinesia.
† One patient had both ventricular akinesia and aortic atheromatosis.

results of the ambulatory electrocardiography and was re-evaluated after monitoring was performed. We established in how many patients the detection of paroxysmal atrial fibrillation (PAF) by 24 hr ECG changed the etiologic classification of the stroke and lead to the initiation of anticoagulant therapy. We compared the age of patients with and without PAF using Student's t-test and assessed whether a presentation with a non-lacunar stroke was more frequent in patients with PAF using the χ^2-test.

Results

One hundred seventy seven patients were admitted to the Stroke Unit of the Neurology Department between March and November 2001. Thirty-two patients were excluded because of non-ischemic symptoms (n = 14) or because of TIAs without a hyperintense lesion on DWI (n = 18). This left 145 patients for analysis, 76 men (52.4%) and 69 women (47.6%) with a mean age of 68 (SD 12). One hundred and thirty three of the 145 patients (91.7%) had an ischemic stroke with symptoms lasting longer than 24 hours. Sixty-nine patients had a single lesion and 31 had multiple hyperintense areas on DWI. In 19 patients no hyperintensity was found on DWI. Twelve patients had symptoms lasting less than 24 hours but had one or multiple lesions on DWI.

Standard 12-lead ECG was performed in all patients at admission. Twenty patients had atrial fibrillation. Other major ECG findings were old q-wave infarctions in 14 patients, left ventricular hypertrophy in 5 patients, atrial dilatation in 2 patients and ongoing acute myocardial ischemia with ST-elevation in 1 patient.

One hundred twenty one patients (83.4%) underwent TTE and 107 underwent TEE (73.7%). At least one of these cardiac examinations was performed in 140 patients (96.5%). Significant findings on cardiac and aortic imaging were found in 49 patients (Table 1). A high risk source of cardiac embolism was found in 5 patients (3.6%). These high risk sources were atrial thrombus (n = 1), ventricular tumor (n = 1), dilated cardiomyopathy (1), infectious endocarditis (n = 1) and mitral stenosis (n = 1). Other potential sources of cardiac embolism were found in 44 patients (31.4%).

Twenty-seven patients presented with a total anterior circulation infarct (TACI, 18.6%), 34 had a partial anterior circulation infarct (PACI, 29.7%), 43 (29.7%) had a lacunar infarct (LACI) and 36 had a posterior circulation infarct (POCI, 24.8%). In 5 patients an accurate clinical classification was impossible. The etiologic classification according to the TOAST criteria is shown in Table 2.

Ambulatory electrocardiography was performed in 136 (94%) patients, 69 men and 67 women. Ambulatory electrocardiography was performed a median of 3 days (25^{th} percentile-75^{th} percentile, 2–4) after admission. Nine patients did not receive a Holter, either because the etiology was already defined (n = 8) or the ambulatory electrocardiography had already been performed in another institution (n = 1).

In 29 of the 136 patients (21.3%) intermittent or persistent AF was recorded. Other major findings on Holter monitoring were episodes of sinus blockade lasting between 2 and 3 seconds in 4 patients (2.9%). Persistent AF was already identified in 20 of these patients from the ECG obtained at admission. Paroxysmal atrial fibrillation was diagnosed in 9 patients on Holter examination. Two of the

Table 2

Etiologic classification (TOAST)

TOAST subtype	Number of patients (%)
Cardioembolic	
Probable	33 (22.7%)
Possible	18 (12.4%)
Large Artery Disease	25 (17.2%)
Small vessel disease	31 (21.4%)
Other Determined Etiology	4 (2.8%)
Undetermined	
Incomplete Evaluation	3 (2.1%)
Complete Evaluation	13 (9.0%)
2 possible Etiologies	18 (12.4%)

9 patients had a previous history of PAF. In 7 patients (5.2%) paroxysmal atrial fibrillation was not suspected from the medical history and accidentally discovered by ambulatory electrocardiography (Table 2). Both TTE and TEE were performed in 5 of these 7 patients and TTE alone in one patient. One patient underwent TEE alone. Examination showed hypokinesia of the left ventricle in one patient. Three patients had mild atherosclerosis of the aorta and four patients had mild to moderate atrial dilatation. In one patient spontaneous echo contrast was found on TEE. In one patient the TEE was completely normal.

We did not find a significant difference in age between the groups with and without paroxysmal AF ($p = 0.12$). There was also no evidence of a higher frequency of non-lacunar strokes in the group with paroxysmal AF ($p = 0.4$). In the 7 patients with previously unsuspected PAF, the TOAST etiology changed from cryptogenic with complete evaluation to a cardioembolic etiology in three patients. In four patients the TOAST classification changed from a single cause to multiple potential etiologies. Three patients had small vessel disease and one patient had hypokinesia of the left ventricle and a 50-75% stenosis of the ipsilateral internal carotid artery as other possible causes for stroke. The secondary prevention measure changed from antiplatelet therapy to oral anticoagulation in 6 out of 7 patients. In 1 patient oral anticoagulants were contraindicated.

Discussion

The impact of ambulatory electrocardiography in a standard stroke workup remains controversial. In our study 5.1% of stroke patients had paroxysmal AF discovered on 24 hour ECG monitoring, which was not previously known by history or detected on routine ECG at admission. Secondary prevention measures with antiplatelets changed in almost all patients to oral anticoagulation therapy.

Few publications have assessed the impact of ambulatory electrocardiography as a diagnostic test in ischemic stroke. Previous studies generally found a relatively low yield of ambulatory electrocardiography. One study found significant cardiac arrhythmias in only 1 out of 20 patients (Fisher, 1978). A larger study performed ambulatory electrocardiography only in a selected subset of 184 TIA and stroke patients. Previously unknown AF was found in 3 out of 55 patients (Rem, Hachinski, *et al.*, 1985). A Dutch study detected one case of AF among 100 patients with transient cerebral ischemia (Koudstaal, van Gijn, *et al.*, 1986). In another study, 15 of 150 patients had AF on ambulatory electrocardiography, but this arrhythmia was already known from the medical history or detected on routine ECG in all cases (Come, Riley, *et al.*, 1983). A few studies found a rate of unsuspected AF similar to ours. A German study detected 7 new cases of paroxysmal AF by 24hour ECG, performed in 135 stroke patients (Richardt, Ensle, *et al.*, 1989). In the largest study 15 out of 312 patients (5.4%) had PAF on ambulatory electrocardiography (Norris, Froggatt, *et al.*, 1978).

Our study has several limitations. The sample size was small and we were therefore not able to identify subgroups in whom ambulatory electrocardiography has a higher yield. We found no evidence of a higher frequency of nonlacunar syndromes among patients with PAF, but the study had insufficient power to detect a difference. We only included patients with TIA who had an area of hyperintensity on DWI to exclude non-vascular symptoms and this might have increased the detection of abnormalities on 24 hr ECG. It is unclear if routine continuous cardiac monitoring early after admission would have provided the same information. In one of the patients the episode of AF was short and this arrhythmia would easily have been overlooked on a cardiac monitor. We did not include a control group of age and sex matched healthy individuals to prove that AF was not an incidental finding in some of these patients. Also, it is unclear if the PAF did not occur as a result of the cerebral abnormality (Norris, Froggatt, *et al.*, 1978 ; Vingerhoets, Bogousslavsky, *et al.*, 1993). Data from the Framingham study suggest that most patients in whom paroxysmal atrial fibrillation is detected at the onset of stroke converts to chronic atrial fibrillation or is recurring (Lin, Wolf, *et al.*, 1995). No randomised controlled trials have been performed that specifically assessed whether oral anticoagulation is superior to aspirin in patients with paroxysmal atrial fibrillation, whereas the evidence favouring carotid endarterectomy in patients with symptomatic high grade carotid artery stenosis is conclusive (Anonymous, 1991 ; Anonymous, 1998). Data from the SPAF studies however suggest that patients with PAF who are treated with aspirin have

Table 3

Demographic and clinical characteristics of patients with unsuspected atrial fibrillation on 24hr ECG

Sex	Age (Years)	Duration of PAF on Holter	Clinical subtype (Bamford)	Ventricular response rate of AF (beats per minute, range)	TOAST subtype prior to Holter and after Holter	Therapy
F	86	Frequent episodes	TACI	46-153	Cryptogenic → Cardioembolic	OAC
F	79	Several hours	LACI	36-116	Small vessel disease → Cryptogenic (2 causes)	OAC
F	79	Several hours	LACI	40-132	Small vessel disease → Cryptogenic (2 causes)	ASA
F	81	Several hours	LACI	55-140	Small vessel disease → Cryptogenic (2 causes)	OAC
F	74	Frequent episodes	PACI	54-216	Cryptogenic → Cardioembolic	OAC
M	35	1 run	PACI	Max. 103	Cryptogenic → Cardioembolic	OAC
M	71	Several hours	PACI	70-160	Cryptogenic (2 causes)* → Cryptogenic	OAC

OAC = anticoagulation ; ASA = acetylsalicyl acid ; TACI, PACI, LACI and POCI : Bamford-classification
* A high-grade carotid stenosis (50-70% reduction in diameter) was present as well as a hypokinetic left ventricle on echocardiography.

the same rates of recurrent stroke as patients with persistent AF treated with aspirin (Hart, Pearce, *et al.*, 2000). A recent meta-analysis of six randomized trials of antithrombotic agents in atrial fibrillation concluded that the recurrent stroke rate is significantly lower when patients with paroxismal atrial fibrillation are treated with oral anticoagulants rather than with aspirin (van Walraven, Hart, *et al.*, 2002).

In conclusion, we found that ambulatory electrocardiography increases the detection of paroxysmal atrial fibrillation and changes the antithrombotic strategy. Further prospective studies are needed to identify subtypes of patients in whom the yield of ambulatory electrocardiography is higher.

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